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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/600,648 | 10/17/2000 | Shalaby Wahba Shalaby | 00537-165002 | 9033 |

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| EXAMINER | |
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1651 | |

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/600,648 | SHALABY, SHALABY WAHBA | |
| | Examiner | Art Unit | |
| | David M. Naff | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/20/06 has been entered.

The submission presented an Information Disclosure Statement, and did not amend the claims finally rejected in the previous office action of 6/9/06.

Claims examined on the merits are 1-48, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 112***

Claims 1-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Description is not found in the specification of the protein or peptide being "ionically immobilized, but not conjugated" as required in claims 1 and 12. If ionically immobilized, the protein or peptide

is attached to the surface, and is inherently conjugated to the surface when conjugated is given its normal and accepted meaning.

***Claim Rejections - 35 USC § 112***

Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are unclear as to how the protein or peptide can be ionically immobilized, but not conjugated, on the surface. Description is not found in the specification of the protein or peptide being ionically immobilized on the surface, and at the same time not being conjugated to the surface. The term "conjugated" when given its normal and accepted usage means attached to the surface. Ionically immobilizing on the surface attaches the protein or peptide to the surface, and how this attaching to the surface can occur without being "conjugated" is not understood.

The claims are confusing and unclear as to the relationship of the core to the microparticle. The portion of the microparticle that is the core and not the core is unclear. Additionally, it is unclear how a core can have a surface as in line 6 of claim 1 and be comprised by a microparticle.

Claim 12 is confusing and redundant by requiring the microparticle of claim 1, and then again repeating what the microparticle comprises. Additionally, the description of the microparticle in claim 12 is different from that in claim 1. It is

suggested that claim 12 be amended by changing the comma at the end of line 3 to a period, and cancel all of the claim following the period.

Claim 1 in confusing and unclear by not having clear antecedent basis for "the therapeutic" in the third line from the last line. The claim has not previously required the protein or peptide to be therapeutic.

***Response to Arguments***

A response of 3/20/06 urged that the specification discloses that "polymer core" is another way of referring to microparticles. If the microparticle and the core are the same, a microparticle cannot comprise a core. Using two different terms in a claim to set forth the same component confuses and beclouds the metes and bounds of the invention claimed. It is suggested claim 1 be amended by canceling "core" in lines 2 and 6, canceling ", but not conjugated," in line 4, after "surface" in line 4, insert --- of said microparticle, and said surface comprising crevices, ---, cancel lines 5-8, and in the third line from the last line cancel "therapeutic". Any dependent claim should be amended to be consistent with these amendments to claim 1, if required.

***Claim Rejections - 35 USC § 103***

Claims 1-11, 22, 23, 26-33 and 47 rejected under 35 U.S.C. 103(a) as being unpatentable over Shalaby et al (5,672,659) or Ignatious et al (WO 97/39738) in view of Shalaby (5,612,052) and Chesterfield et al (5,366,756).

The claims are drawn to a microparticle comprising an absorbable heterochain polymer core and one or more peptides and/or proteins ionically immobilized, but not conjugated, on the surface, and crevices formed on the surface. The protein or peptide is released over an extended period of time in a patient.

Shalaby et al ('659) and Ignatious et al disclose a composition containing a carboxyl group-containing polymer that can be a heterochain polymer ionically conjugated (col 2, line 65 of Shalaby et al and page 1, line 23 of Ignatious et al) with a bioactive polypeptide or a drug that is a polypeptide. The conjugate may be formed into microparticles. The conjugate is formed by combining a solution of the polymer with a solution of the polypeptide. See cols 2 and 3 of Shalaby et al and pages 4-9 of Ignatious et al. The polypeptide undergoes sustained release in a patient (Shalaby et al, col 1, lines 12-13).

Shalaby et al ('052) discloses coating microparticles with a drug to provide controlled release of the drug (col 7, lines 30-33).

Chesterfield et al disclose polymer particles coated with a tissue growth promoter and if desired a therapeutic agent for implanting to repair tissue (cols 1-3).

The present invention differs from Shalaby et al ('659) and Ignatious et al in that in the claims the protein or peptide is immobilized, but not conjugated, on the microparticle surface having crevices, whereas Shalaby et al and Ignatious et al form the conjugate

by combining solutions of the polymer and polypeptide, and forming a microparticle containing the polypeptide.

It would have been obvious to form the polymer of Shalaby et al ('659) or Ignatious et al into a microparticle prior to conjugating with the polypeptide or protein as suggested by Shalaby et al ('052) and Chesterfield et al forming a polymer microparticle and immobilizing a drug and/or growth promoter on the microparticle. Forming the microparticle before binding the polypeptide would have been expected to provide the polypeptide on the surface of the microparticle and make it more readily available. Microparticles formed as disclosed by Shalaby et al ('659) or Ignatious et al will inherently have some crevices on the surface since present specification discloses no conditions needed to form crevices when forming the microparticles. The protein or peptide not being conjugated to the surface as required in the claims is merely a matter of individual interpretation of how immobilizing occurs. When obviously immobilizing the polypeptide of Shalaby et al ('659) or Ignatious et al on the surface of microparticles rather than in microparticles, it would have been obvious to ionically immobilize the polypeptide to the surface since Shalaby et al ('659) and Ignatious et al ionically attach the polypeptide to the polymer. The conditions of dependent claims are disclosed by the references, or would have been obvious from conditions disclosed by the references.

***Response to Arguments***

The response of 3/20/06 urged that the polypeptide being ionically conjugated to the polymer as disclosed by Shalaby et al ('659) or Ignatious et al is inconsistent with complexes of the instant application. However, when ionically immobilized, the protein or peptide of the claims is immobilized in the same way as when obviously immobilizing the polypeptide of Shalaby et al ('659) or Ignatious et al on a microparticle surface as set forth above. Requiring ionic immobilization to not be conjugating is a coined definition of immobilizing that has no basis in the present specification. Shalaby et al ('659) and Ignatious et al are using the term "conjugate" merely to denote that the polypeptide is attached to the polymer. Conjugated is apparently being used in the claims in a way contrary to this normal usage. The present specification nowhere describes how the protein or peptide can be ionically immobilized on the surface of the microparticle, and at the same time not be attached to the surface.

The response urged that microparticles of the present invention are formed in a heterogeneous system and do not result in a homogenous ionic species as in Shalaby et al ('659) or Ignatious et al. However, the claims do not require a heterogeneous system other than a heterochain polymer. Shalaby et al ('659) and Ignatious et al disclose a heterochain polymer.

***Claim Rejections - 35 USC § 103***

Claims 12-21, 24, 25, 34-46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claims 1-11, 22, 23, 26-33 and 47 above, and further in view of Auer et al (WO 92/11844) and Demian et al (5,795,922).

The claims require the bound microparticle containing the immobilized protein or polypeptide to be encased.

Auer et al disclose forming a complex of a protein pharmaceutical agent and a polycationic reagent, and encapsulating the complex in a microsphere (pages 4-9) to provide sustained release of the protein.

Demian et al disclose microencapsulating radiopacifier particles to prevent agglomerating (col 3).

When modifying Shalaby et al ('659) or Ignatious et al by forming the polymer into a microparticle before binding the polypeptide as set form above, it would have been obvious to encapsulate the polypeptide-containing microparticle as suggested Auer et al to provide sustained release and as suggested by Demian et al to prevent agglomerating.

***Response to Arguments***

The response urged that the present claims are dependent on claims that are unobvious. However, for reasons set forth above, the claims on which the present claims depend are still considered obvious.

***Conclusion***

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114

and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
9/1/06